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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,551	03/31/2004	Ronald W. Barrett	34545/US/4/AMP/SKS	9974

20686 7590 05/28/2008

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
05/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,551	BARRETT ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

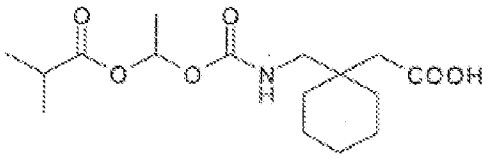
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/4/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group II, claims drawn to a method for treating or preventing hot flashes in a patient comprising adminsitering to the patient in need of such treatment or prevention a therapeutically effective amount of a prodrug of a GABA analog, or a pharmaceutically acceptable salt, hydrate or solvate thereof with elected species **gabapentin enacarbil** also known as XP 13512 as a specific prodrug of the GABA analog gabapentin is acknowledged.

The structure of the elected species is depicted below:



Claims 1-17, 19 and 20 have been examined only to the extent of applicants' elected species. Claim 18 has been withdrawn from consideration since it is drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-17, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treating hot flashes", does not reasonably provide enablement for the "**preventing** hot flashes". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method of treating or preventing hot flashes in a patient comprising administering to the patient in need of such treatment or prevention a therapeutically effective amount of a prodrug of a GABA analog, or a pharmaceutically acceptable salt, hydrate or solvate thereof. The nature of the invention is extremely complex in that it encompasses the **actual prevention** of hot flashes such that the subject treated with above compounds does not contract hot flashes.

Breath of the Claims: The complex of nature of the claims

greatly exacerbated by breath of the claims. The claims encompass prevention of hot flashes in humans which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent hot flashes is minimal. All of the guidance provided by the specification is directed towards **treatment rather than prevention** of hot flashes.

Working Examples: All of the working examples provided by the specification are directed toward the **treatment rather than prevention** of hot flashes.

State of the Art: While the state of the art is relatively high with regard to treatment of hot flashes, the state of the art with regard to **prevention** of such disorders is underdeveloped. The Role of Serotonin in Hot Flushes by Hemmie H.G. Berendsen, Maturitas (2000) 36 (1): 155-164), teaches that 80% of all women experience hot flushes as a aprt of menopause, with 40%seeking medical help, and also teaches that such flushes may occure after bilateral ovariectomy and in premenstrual syndrome (see page 155, in particular). The reference teaches that the exact pathophysiology of the hot flushes is still unknown, although estrogens are believed to play a role (see page 156, in particular). Thus, the exact pathophysiology of hot flaushes are not known.

Therefore, the method comprising actual prevention of hot flushes with unknown pathophysiology is highly speculative.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of hot flashes in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of **prevention** of hot flashes.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for prevention of hot flashes. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of hot flashes with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of hot flashes with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the

claimed invention to prevent the development of hot flashes in a subject by administration of one of the claimed compounds.

Therefore, a method of treating or preventing hot flashes in a patient comprising administering to the patient in need of such treatment or prevention a therapeutically effective amount of a prodrug of a GABA analog, or a pharmaceutically acceptable salt, hydrate or solvate thereof is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guttuso, Jr. (U.S.Patent No. 6,310,098 B1) of record in view of R & D Focus Drug News (9 Dec. 2002).

Guttuso, Jr. teaches method of treating hot flashes comprising administering gabapentin in a male or female. (abstract, columns 7 and 8, Example 2).

Guttuso, Jr. teaches that hot flashes or flushing occur commonly in menopausal women but men may also have hot flashes following androgen deprivation therapy (from bilateral orchiectomy or treatment with a gonadotrophin-releasing-hormone agonist) for metastatic prostate cancer. (column 1, lines 15-37).

Guttuso, Jr. does not expressly teach employment of gabapentin enacarbil for the treatment of hot flashes, specific amounts, and the specified dosage formulations.

R & D Focus Drug News teaches Gabapentin XP (also known as gabapentin enacarbil) is a prodrug of gabapentin. R & D Focus Drug News teaches gabapentin enacarbil demonstrated dose-proportional blood levels of active gabapentin, following oral administration and it is better absorbed into the colon than gabapentin itself.

It would have been obvious to one of ordinary skill in the art to employ Gabapentin XP for the treatment of hot flashes in men or woman because R & D Focus Drug News teaches that Gabapentin XP is a prodrug of gabapentin and because it has advantages over gabapentin by exhibiting better absorption into the colon than gabapentin. One would have been motivated to make such a modification in order to achieve expected benefit of "prodrug" of gabapentin well known to one of ordinary skill in the art that converts to active form, i.e. gabapentin in human body. There is a reasonable expectation of success in treating hot flashes comprising administering Gabapentin XP to men or woman suffering from hot flashes because Gabapentin is known in the art by Guttuso, Jr. for having effectiveness in treating hot flashes and because Gabapentin XP is a prodrug of Gabapentin converts to Gabapentin in vivo as taught by R & D Focus Drug News. The amounts of active agents to be used, the pharmaceutical forms, e.g., tablets, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
May 21, 2008